UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/398,253	09/17/1999	MICHAEL NEHLS	8535-026-999	9822

20583 7590 11/05/2002

PENNIE AND EDMONDS
1155 AVENUE OF THE AMERICAS
NEW YORK, NY 100362711

EXAMINER	
KIM, YOUNG J	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 11/05/2002 21

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/398,253	Applicant(s) NEHLS ET AL.	
	Examiner Young J. Kim	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 August 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,10 and 11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,10 and 11* is/are rejected.

7)☒ Claim(s) *11* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Written Description Example 9* .

DETAILED ACTION

The prosecution for the instant application has been hereby reopened in order to address all of the issues raised in the Appeal Brief received on August 5, 2002 (Paper No. 20).

Claims Objection

Applicants are advised that claim 11 is objected to for depending on a non-elected claim (claim 5). For the purpose of prosecution, the phrase that reads, "an oligonucleotide of Claim 1, 3, 4, or 5" has been assume to read, "an oligonucleotide of Claim 1, 3, 4, or 10".

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10 is indefinite for the recitation of the phrase, "at least one of SEQ ID NOS: 16," because only one SEQ ID Number is recited rendering the claim indefinite in whether more SEQ ID Numbers ought to be included.

Claim Rejections - 35 USC § 101 & 112 first paragraph-Enablement

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The rejection of claims 1, 3, 4, 10, and 11 under 35 U.S.C. 101 because the claimed invention lacks patentable utility due to its not being supported by either specific and/or substantial utility or a well established utility, in the Office Action mailed on July 3, 2001 is maintained for the reasons of record.

Applicants' arguments filed in the Appeal Brief received on August 5, 2002 have been fully considered but they are not found persuasive.

Applicants' arguments have been addressed in the order they were presented.

Applicants state that the Federal Circuit has stated that "(t)o violate § 101 the claimed device must be totally incapable of achieving useful result." (pp. 6).

However, the instant situation is analogous to that which was addressed in *Brenner v. Manson*, 148 USPQ 689 (1966), wherein the court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. 101, which requires that an invention must have either an **immediately apparent** or fully disclosed "real world" utility (emphasis added). The court held that:

"The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility...[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form there is insufficient justification for permitting an appellant to engross what may prove to be a broad field...a patent is not a hunting license...[i]t is not a reward for the search, but compensation for its successful conclusion.

Applicants contend that the sequences set forth in SEQ ID Nos: 9-18 are not identified from the human genome randomly, rather, they represent a selection of genetic sequences that play a role in the later stages of cellular differentiation and development based on the fact that although the gene trap vectors "disrupt" exons of a gene, such disruptions have not hampered the growth of the cell in cell cultures (pp. 8).

It appears that whether the sequences set forth in SEQ ID Nos: 9-18 actually play a role in the later stages of cellular differentiation and development is a speculation based on the fact that the cells containing such disruptions were viable regardless. The specification makes no disclosure of evidence disclosing such assertion. Even if Applicants' assertions were true in that the sequences set forth in SEQ ID Nos: 9-18 played a role in the later stages of cellular differentiation and development, Applicants have not disclosed what such roles were. It is clear that the claimed sequences do not have a substantial utility because the sequences are **not** "refined and developed to this point-where specific benefit exists in currently available form," requiring further experimentation of a skilled practitioner. As stated above, the court expressed that a patent, "is not a reward for the search, but compensation for its successful conclusion." Applicants have not arrived at such successful conclusion of how the claimed sequences are involved in the cellular differentiation and development, but rather arrived at a starting point of further research in determining how the claimed sequences are actually involved.

Applicants state that the Examiner of record appeared to contend (in the Advisory Action mailed on January 29, 2002) that the claimed nucleic acids do not have specific utility because the nucleic acids lack a substantial utility (pp. 8). Without acquiescing to the allegation, the statement addressed the fact that although the claimed nucleic acids might be specific to their

targets (as all nucleic acids are specific to their complements), the issue at hand was the fact that the claimed nucleic acids did not have a substantial utility.

Applicants state that because teratocarcinomas are totipotent, in that they may differentiate into many different cell types (such as teeth, hair, bone, muscle and cartilage) along various pathways upon induction by certain signals, the claimed oligonucleotides and polynucleotides can be used as probes to "**determine the activity** at the genetic loci during development and differentiation of the teratocarcinomas" (pp. 9, 1st paragraph).

It is clear from even the Applicants' response that the claimed oligonucleotides can only be used to further study (or to determine) the genes to which they hybridize to. Other than the speculation that the genes to which the claimed oligonucleotides hybridize to might be involved in a development and differentiation activity, Applicants clearly have not arrived at the "successful conclusion" of what the actual function of the gene is or how such gene is involved in the development and differentiation of teratocarcinomas. Without such knowledge, it would only serve as a starting point of further experimentation to arrive at the "successful conclusion" as expressed by the court.

Applicants also state that the claimed polynucleotide or oligonucleotides of the invention can also be used for diagnostic gene expression and analysis, for cross species hybridization analysis, antisense inhibition, gene therapy, gene delivery, etc.

Although such utilities are well known in the art, the claimed polynucleotides or oligonucleotides would not have a substantial utility as listed because the specification does not give a substantial, conclusive evidence for applying the claimed polynucleotides or oligonucleotides. In other words, Applicants have not provided what condition a skilled

practitioner is to look for when conducting a "diagnostic gene expression," or what is to be benefited from inhibiting the expression of the gene to which the claimed oligonucleotides hybridize to, or what condition is to be alleviated in applying the claimed oligonucleotides/polynucleotides in a gene therapy, or why the claimed oligonucleotides/polynucleotides should be delivered. A successful conclusive disclosure, or an immediately apparent utility (or a substantial utility) would allow a skilled practitioner to be able to answer the above questions based on the disclosure. The disclosure of the instant application, however, fails to disclose such utility.

Applicants also argue that the claimed nucleic acid detects an upregulation of nucleic acid 'a' in teratocarcinoma cells at a particular stage of differentiation and development and that one of ordinary skill in the art would infer that a nucleic acid 'a' plays a role in the differentiation and development of the cells at that particular stage or in that stage (pp. 10). This argument requires the artisan to **conduct further research** on the nucleic acid to be able to determine exactly what role the nucleic acid plays and at which stage of differentiation and development. The instant specification provides no more than a starting point for the practitioner to conduct research to arrive at the "immediately apparent" utility.

Finally, Applicants argue that the gene trapped sequences of the present invention overcomes some of the limitations of conventional cDNA and EST libraries because the, "claimed oligonucleotide and polynucleotide sequences were identified using gene trap vectors that do not rely solely on the level of endogenous mRNA expression of a gene for identification of that gene" thereby being able to trap even the poorly expressed genes. Although the gene trap

vectors might be able to trap even the poorly expressed genes, such isolated nucleic acid must also fulfill the utility requirement as illustrated above.

For the foregoing reasons, the utility rejection is maintained.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 1, 3, 4, 10, and 11 under 35 U.S.C. 112, first paragraph because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above in the Office Action mailed on July 3, 2001 is maintained for the reasons of record.

Applicants' arguments filed in the Appeal Brief received on August 5, 2002 have been fully considered but they are not found persuasive as illustrated above.

The rejection of claims 1, 3, 4, 10, and 11 under 35 U.S.C. 112, first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention in the in the Office Action mailed on July 3, 2001 is maintained for the reasons of record.

Applicants' arguments filed in the Appeal Brief received on August 5, 2002 have been fully considered but they are not found persuasive.

Applicants' arguments have been addressed in the order they were presented.

Applicants argue that the synthetic oligonucleotides or isolated polynucleotides are fully described by structure or by physical properties, or both, sufficient to distinguish the claimed synthetic oligonucleotides or isolated polynucleotides from other materials. Applicants use claim 1 as an example, wherein the claim recites that the synthetic oligonucleotides comprise a contiguous stretch of at least nucleotides of at least one of the elected SEQ ID Numbers. Applicants argue that although there are numerous oligonucleotides that falls within this description, one of ordinary skill in the art can readily recognize the synthetic claim as described in claim 1.

The claim as written, however, reads on 1) a synthetic oligonucleotide that is a full-length cDNA or 2) a full-length cDNA which hybridizes to the claimed oligonucleotides. As already indicated in the previous Office Action, Applicants have not disclosed the full-length open reading frame from which the oligonucleotide is derived from or hybridize to. Because a skilled practitioner would not be able to, even with the prior art disclosure, envision the un-described sequences contained by a full-length cDNA or a gene sequence, the claims of the present invention fails to describe the invention as claimed.

Although claim 11 is drawn to a nucleic acid which hybridizes to the oligonucleotides under a specific conditions, the claims lack the functional characteristics coupled with a known or disclosed correlation between function and structure. Consequently, claims read on nucleic acids with any function that would hybridize to the claimed oligonucleotide because the genus of such nucleic acids is highly variant, rendering the claims lacking in their written description (See Written Description Guideline, Example 9, attached hereto).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Duncan et al. (EP 505605-A, September 1992).

Claim 1 is drawn to an oligonucleotide comprising a contiguous stretch of at least about 15 nucleotides of at least one of SEQ ID Numbers 9-13, 15, 17, and 18.

Duncan et al. disclose a nucleic acid probe (or oligonucleotide) that exhibits 15 contiguous nucleotides of SEQ ID Number 9 (See Homology Search Result).

Therefore, Duncan et al. anticipate the invention as claimed.

Claim 1, 3, and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Zhao et al. (GenBank Accession Number AQ534984, direct submission 1997).

Claim 1 is drawn to an oligonucleotide comprising a contiguous stretch of at least about 15 nucleotides of at least one of SEQ ID Numbers 9-13, 15, 17, and 18.

Claim 3 is drawn to an isolated polynucleotide comprising a contiguous stretch of at least 60 nucleotides of at least one of SEQ ID NOS: 9-18.

Claim 11 is drawn to an isolated polynucleotide capable of hybridizing to the oligonucleotide or the polynucleotide of claims 1, 3, 4, or *5* (*sic*) under high stringent conditions.

Zhao et al. disclose a nucleic acid sequence comprising 123 contiguous nucleotides of SEQ ID NO: 15 (See Sequence Homology Result).

The nucleic acid disclosed by Zhao et al. exhibits 99% overall homology to that of SEQ ID NO: 15, thereby being capable of hybridizing to the nucleic acid/oligonucleotide comprising SEQ ID NO: 15.

In order to give scientific evidence for the basis of this rejection, melting temperature of the cited nucleic acid had been calculated based on the formula (pp. 269, formula number 5) disclosed in Meinkoth et al., "Hybridization of nucleic acids immobilized on solid supports," (Analytical Biochemistry, 1984, vol. 138, pp. 267-284). The melting temperature of the cited nucleic acid was calculated under the most stringent wash condition set forth in the claim (2.0x SSC at 50^{o}C). The salt concentration (in molarity) was calculated based on the disclosure by Meinkoth et al. (pp. 267, footnote), resulting in 0.5 M of sodium concentration. The resulting melting temperature was calculated to be 92.9^{o}C. Based on this calculation, the cited nucleic acid has a melting temperature that is above the claimed incubation temperature, thus fully capable of being hybridized to nucleic acid of SEQ ID Number 15, rendering the claim anticipated.

Therefore, Zhao et al. anticipate the invention as claimed.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Kaushansky (WO 95/21626-A1, August 17, 1995).

Kaushansky discloses a nucleic acid that exhibits 21 contiguous nucleotides of SEQ ID Number 18 (See Homology Search Result).

Therefore, Kaushansky anticipates the invention as claimed.

No claims are allowed.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (703) 308-9348. The Examiner can normally be reached from 8:30 a.m. to 7:00 p.m. Monday through Thursday. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Benzion, can be reached at (703) 308-1119. Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. The Fax number is (703) 746-3172. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Young J. Kim

10/29/02

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

10/30/02